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=> d his

     (FILE 'HOME' ENTERED AT 08:41:54 ON 21 NOV 2002)

     INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,
     BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,
     CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB,
     DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 08:42:03 ON
     21 NOV 2002
               SEA FUCOSYLTRANSFERASE
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                4   FILE ADISALERTS
                1   FILE ADISNEWS
               50   FILE AGRICOLA
               14   FILE ANABSTR
                4   FILE AQUASCI
                3   FILE BIOBUSINESS
                5   FILE BIOCOMMERCE
             1230   FILE BIOSIS
              116   FILE BIOTECHABS
              116   FILE BIOTECHDS
              627   FILE BIOTECHNO
              101   FILE CABA
              465   FILE CANCERLIT
             1353   FILE CAPLUS
               15   FILE CEABA-VTB
                2   FILE CEN
               49   FILE CONFSCI
               12   FILE DDFB
               20   FILE DDFU
              436   FILE DGENE
               12   FILE DRUGB
               24   FILE DRUGU
                9   FILE EMBAL
              983   FILE EMBASE
              531   FILE ESBIOBASE
               18   FILE FEDRIP
                2   FILE FROSTI
                7   FILE FSTA
              890   FILE GENBANK
               75   FILE IFIPAT
              165   FILE JICST-EPLUS
              280   FILE LIFESCI
             1117   FILE MEDLINE
                1   FILE NIOSHTIC
                2   FILE NTIS
              325   FILE PASCAL
                1   FILE PHIN
                5   FILE PROMT
              995   FILE SCISEARCH
              250   FILE TOXCENTER
              280   FILE USPATFULL
                2   FILE USPAT2
               66   FILE WPIDS
               66   FILE WPINDEX
L1              QUE FUCOSYLTRANSFERASE
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     FILE 'CAPLUS, BIOSIS, MEDLINE, SCISEARCH, EMBASE, BIOTECHNO, ESBIOBASE,
     CANCERLIT' ENTERED AT 08:43:19 ON 21 NOV 2002
L2          1355 S L1 AND (LEWIS X)
L3           100 S L2 AND HELICOBACTER
L4            40 S L3 AND (ISOLAT? OR PURIF? OR CDNA OR CLONE)
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L5 15 DUP REM L4 (25 DUPLICATES REMOVED)

=> d l5 ibib ab 10-15

L5 ANSWER 10 OF 15 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1998:746829 SCISEARCH
THE GENUINE ARTICLE: 122RN
TITLE: Human alpha 1,3/4-**fucosyltransferases** - III. A Lys/Arg residue located within the alpha 1,3-FucT motif is required for activity but not substrate binding
AUTHOR: Sherwood A L; Nguyen A T; Whitaker J M; Macher B A; Stroud M R; Holmes E H (Reprint)
CORPORATE SOURCE: NW HOSP, PACIFIC NW CANC FDN, DIV CELL SURFACE BIOCHEM, 120 NORTHGATE PLAZA, SUITE 218, SEATTLE, WA 98125 (Reprint); NW HOSP, PACIFIC NW CANC FDN, DIV CELL SURFACE BIOCHEM, SEATTLE, WA 98125; SAN FRANCISCO STATE UNIV, DEPT CHEM & BIOCHEM, SAN FRANCISCO, CA 94132
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (25 SEP 1998) Vol. 273, No. 39, pp. 25256-25260.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 36
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Amino acid sequence alignment of human alpha 1,3/4-**fucosyltransferases** (FucTs) demonstrates that three highly conserved Lys residues are present in the catalytic domain of FucTs III, TV, V, and VI. Two of these sites are conserved in FucT VII, with the third located within the alpha 1,3-FucT motif as a conservative change to Arg at position 223. Site-directed mutagenesis experiments were conducted to change Lys(255) Of FucT V (equivalent to Arg(223) of FucT VII) to either Arg(255) or Ala(255). Enzyme assays demonstrate that the FucT V K255R mutant has a 34-fold lower specific activity than native FucT V and that the K255A mutant is inactive. Site-directed mutagenesis of FucT VII was also conducted to change Arg(223) to Lys(223) for analysis of the effect on enzyme kinetic parameters. No differences in acceptor specificities or K-m values for either substrate were observed between native FucT VII and the R223K mutant; however, the **purified** R223K mutant enzyme had a 2-fold increased specific activity compared with **purified** native FucT VII. No change in GDP-fucose-protectable pyridoxal-P/NaBH4 inactivation was observed for native or mutant FucT V or VII, further supporting the absence of involvement of this residue in sugar nucleotide binding. The results indicate that a basic residue in this position is required for enzyme activity, with a Lys residue providing higher intrinsic activity. The lack of influence of this site on substrate binding parameters and its location within the alpha 1,3-FucT motif suggest that at least some of the residues within this motif are involved in catalysis rather than substrate binding.

L5 ANSWER 11 OF 15 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1998:642782 SCISEARCH
THE GENUINE ARTICLE: 111MB
TITLE: Molecular cloning and characterization of an alpha 1,3 **fucosyltransferase**, CEFT-1, from Caenorhabditis elegans
AUTHOR: DeBoseBoyd R A; Nyame A K; Cummings R D (Reprint)
CORPORATE SOURCE: UNIV OKLAHOMA, HLTH SCI CTR, DEPT BIOCHEM & MOL BIOL, BRC 417, 975 NE 10TH ST, OKLAHOMA CITY, OK 73104 (Reprint); UNIV OKLAHOMA, HLTH SCI CTR, DEPT BIOCHEM & MOL BIOL, OKLAHOMA CITY, OK 73104
COUNTRY OF AUTHOR: USA
SOURCE: GLYCOBIOLOGY, (SEP 1998) Vol. 8, No. 9, pp. 905-917.

Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
ISSN: 0959-6658.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 54

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We report on the identification, molecular cloning, and characterization of an alpha 1,3 **fucosyltransferase** (alpha 1,3FT) expressed by the nematode, Caenorhabditis elegans, Although C. elegans glycoconjugates do not express the **Lewis x** antigen Gal beta 1-->4[Fuc alpha 1-->3]GlcNAc beta-->R, detergent extracts of adult C,elegans contain an al,3FT that can fucosylate both nonsialylated and sialylated acceptor glycans to generate the Le(X) and sialyl Le(X) antigens, as well as the lacdiNAc-containing acceptor GalNAc beta 1-->4GlcNAc beta 1-->R to generate GalNAc beta 1-->4 [Fuc alpha 1-->3]GlcNAc beta 1-->R. A search of the C. elegans genome database revealed the existence of a gene with 20-23% overall identity to all five cloned human alpha 1,3FTs. The putative **cDNA** for the C,elegans alpha 1,3FT (CEFT-1) was amplified by PCR from a **cDNA** lambda ZAP library, cloned, and sequenced. COS7 cells transiently transfected with **cDNA** encoding CEFT-1 express the Le(X), but not sLe(X) antigen. The CEFT-1 in the transfected cell extracts can synthesize Le(X), but not sialyl Le(X), using exogenous accepters. A second **fucosyltransferase** activity was detected in extracts of C,elegans that transfers Fuc in alpha 1,2 linkage to Gal specifically on type-1 chains. The discovery of alpha-**fucosyltransferases** in C. elegans opens the possibility of using this well-characterized nematode as a model system for studying the role of fucosylated glycans in the development and survival of C,elegans and possibly other helminths.

L5 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4

ACCESSION NUMBER: 1998:7807 CAPLUS
DOCUMENT NUMBER: 128:190186
TITLE: Phase variation in **Helicobacter** pylori lipopolysaccharide
AUTHOR(S): Appelmelk, B. J.; Shiberu, B.; Trinks, C.; Tapsi, N.; Zheng, P. Y.; Verboom, T.; Maaskant, J.; Hokke, C. H.; Schiphorst, W. E. C. M.; Blanchard, D.; Simoons-Smit, I. M.; Van Den Eijnden, D. H.; Vandenbroucke-Grauls, C. M. J. E.
CORPORATE SOURCE: Department of Medical Microbiology, Medical School, Vrije Universiteit, Amsterdam, 1081 BT, Neth.
SOURCE: Infection and Immunity (1998), 66(1), 70-76
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Helicobacter** pylori NCTC 11637 lipopolysaccharide (LPS) expresses the human blood group antigen **Lewis x** (Lex) in a polymeric form. Lex is .beta.-D-galactose-(1-4)-[.alpha.-L-fucose-(1-3)]-.beta.-D-acetylglucosamine. Schematically the LPS structure is (Lex)n-core-lipid A. In this report, we show that Lex expression is not a stable trait but that LPS displays a high frequency (0.2 to 0.5%) of phase variation, resulting in the presence of several LPS variants in one bacterial cell population. One type of phase variation implied the loss of .alpha.1,3-linked fucose, resulting in variants that expressed nonsubstituted polylactosamines (also called the i antigen), i.e., Lex minus fucose; LPS: (lactosamine)n-core-lipid A. The switch of Lex to i antigen was reversible. A second group of variants arose by loss of polymeric main chain which resulted in expression of monomeric Ley; LPS: (Ley)-core-lipid A. A third group of variants arose by acquisition of .alpha.1,2-linked fucose which hence expressed Lex plus Ley; LPS: (Ley)

(Lex)n-core-lipid A. The second and third group of variants switched back to the parental phenotype [(Lex)n-core-lipid A] in lower frequencies. Part of the variation can be ascribed to altered expression levels of glycosyltransferase levels as assessed by assaying the activities of galactosyl-, fucosyl-, and N-acetylglucosaminyltransferases. Clearly phase variation increases the heterogeneity of H. pylori, and this process may be involved in generating the very closely related yet genetically slightly different strains that have been **isolated** from one patient.

L5 ANSWER 13 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 5
ACCESSION NUMBER: 97268464 EMBASE
DOCUMENT NUMBER: 1997268464
TITLE: Cloning and heterologous expression of an .alpha.1,3-**fucosyltransferase** gene from the gastric pathogen **Helicobacter** pylori.
AUTHOR: Ge Z.; Chan N.W.C.; Palcic M.M.; Taylor D.E.
CORPORATE SOURCE: D.E. Taylor, Medical Microbiol./Immunology Dept., 1-28 Medical Sciences Bldg., University of Alberta, Edmonton, Alta. T6G 2H7, Canada. diane.taylor@ualberta.ca
SOURCE: Journal of Biological Chemistry, (1997) 272/34 (21357-21363).
Refs: 56
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Helicobacter** pylori is an important human pathogen which causes both gastric and duodenal ulcers and is also associated with gastric cancer and lymphoma. This microorganism has been shown to express cell surface glycoconjugates including **Lewis X** (Le(X)) and Lewis Y. These bacterial oligosaccharides are structurally similar to tumor-associated carbohydrate antigens found in mammals. In this study, we report the cloning of a novel .alpha.1,3-**fucosyltransferase** gene (HpfucT) involved in the biosynthesis of Le(X) within H. pylori. The deduced amine acid sequence of HpfucT consists of 478 residues with the calculated molecular mass of 56,194 daltons, which is approximately 100 amino acids longer than known mammalian .alpha.1,3/1,4-**fucosyltransferases**. The .apprx.52-kDa protein encoded by HpfucT was expressed in Escherichia coli CSRDE3 cells and gave rise to .alpha.1,3-**fucosyltransferase** activity but neither .alpha.1,4-**fucosyltransferase** nor .alpha.1,2-**fucosyltransferase** activity as characterized by radiochemical assays and capillary zone electrophoresis. Truncation of the C-terminal 100 amino acids of HpFuc-T abolished the enzyme activity. An approximately 72-amino acid region of HpFuc-T exhibits significant sequence identity (40-45%) with the highly conserved C-terminal catalytic domain among known mammalian and chicken .alpha.1,3-**fucosyltransferases**. These lines of evidence indicate that the HpFuc-T represents the bacterial .alpha.1,3-**fucosyltransferase**. In addition, several structural features unique to HpFuc-T, including 10 direct repeats of seven amine acids and the lack of the transmembrane segment typical for known eukaryotic .alpha.1,3-**fucosyltransferases**, were revealed. Notably, the repeat region contains a leucine zipper motif previously demonstrated to be responsible for dimerization of various basic region-leucine zipper proteins, suggesting that the HpFuc-T protein could form dimers.

L5 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
ACCESSION NUMBER: 1997:567080 CAPLUS
DOCUMENT NUMBER: 127:258343
TITLE: **Lewis X** biosynthesis in **Helicobacter** pylori. Molecular cloning of an

.alpha.(1,3)-**fucosyltransferase** gene

AUTHOR(S): Martin, Stephen L.; Edbrooke, Mark R.; Hodgman, T. Charles; Van Den Eijnden, Dirk H.; Bird, Michael I.

CORPORATE SOURCE: Glycobiology Unit, Glaxo Wellcome Medicines Research Centre, Stevenage, SG1 2NY, UK

SOURCE: Journal of Biological Chemistry (1997), 272(34), 21349-21356
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The lipopolysaccharide of certain strains of **Helicobacter** pylori was recently shown to contain the **Lewis X** (Lex) trisaccharide (Gal.beta.-1,4-(Fuc.alpha.(1,3))-GlcNAc). Lex is an oncofetal antigen which appears on human gastric epithelium, and its mimicry by carbohydrate structures on the surface of H. pylori may play an important part in the interaction of this pathogen with its host. Potential roles for bacterial Lex in mucosal adhesion, immune evasion, and autoantibody induction have been proposed (Moran, A. P., Prendergast, M. M., and Appelmelk, B. J. (1996) FEMS Immunol. Med. Microbiol. 16, 105-115). In mammals, the final step of Lex biosynthesis is the .alpha.(1,3)-fucosylation of GlcNAc in a terminal Gal.beta.(1.fwdarw.4)-GlcNAc unit, and a corresponding GDP-fucose:N-acetyl-glucosaminyl .alpha.(1,3) **fucosyltransferase** (.alpha.(1,3)-Fuc-T) activity was recently discovered in H. pylori exts. Part of a human .alpha.(1,3)-Fuc-T amino acid sequence was used to search an H. pylori genomic data base for related sequences. Using a probe based upon weakly matching data base sequences, **clones** from a plasmid library of H. pylori DNA were retrieved. DNA sequence anal. of the library **clones** revealed a gene which was named fucT, encoding a protein with localized homol. to the human .alpha.(1,3)-Fuc-Ts. It has been demonstrated that fucT encodes an active Fuc-T enzyme by expressing the gene in Escherichia coli. The recombinant enzyme shows a strong preference for type 2 (e.g. LacNAc) over type 1 (e.g. lacto-N-biose) acceptors in vitro. Certain residues in a short segment of the H. pylori protein are completely conserved throughout the .alpha.(1,3)-Fuc-T family, defining an .alpha.(1,3)-Fuc-T motif which may be of use in identifying new **fucosyltransferase** genes.

L5 ANSWER 15 OF 15 MEDLINE DUPLICATE 7

ACCESSION NUMBER: 96195860 MEDLINE

DOCUMENT NUMBER: 96195860 PubMed ID: 8608270

TITLE: The biosynthesis of **Lewis X** in **Helicobacter** pylori.

AUTHOR: Chan N W; Stangier K; Sherburne R; Taylor D E; Zhang Y; Dovichi N J; Palcic M M

CORPORATE SOURCE: Department of Chemistry, University of Alberta, Edmonton, Canada.

SOURCE: GLYCOBIOLOGY, (1995 Oct) 5 (7) 683-8.
Journal code: 9104124. ISSN: 0959-6658.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199605

ENTRY DATE: Entered STN: 19960605
Last Updated on STN: 19980206
Entered Medline: 19960530

AB The biosynthesis of the **Lewis X** determinant (Gal beta 1-4 [Fuc alpha 1-3]GlcNAc beta-) in three strains of **Helicobacter** pylori has been investigated. Strains UA 861, UA 802 and UA 1182 contain alpha 1,3 **fucosyltransferase** and beta 1,4 galactosyltransferase activities that synthesize the **Lewis X** structure by

the transfer of monosaccharides from GDP-fucose and UDP-galactose donors, respectively. The enzyme reaction products that formed were characterized by capillary zone electrophoresis and by 1H-NMR spectroscopy. The biosynthetic pathway is therefore identical to that found in humans. In the three strains, the **fucosyltransferase** and galactosyltransferase activities differed in various cellular fractions. Km values for their donor and acceptor substrates also differed.

=> d l5 ibib ab 1-9

L5 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:314468 CAPLUS
DOCUMENT NUMBER: 136:324173
TITLE: Chimeric genes encoding enzymes for biosynthesis of GDP-L-fucose and fucosylated glycans from GDP-D-mannose for treatment of infections and inflammation
INVENTOR(S): Renkonen, Risto; Mattila, Pirkko; Hirvas, Laura; Hortling, Solveig; Kallioinen, Tuula; Kauranen, Sirkka-liisa; Jaervinen, Nina; Maeki, Minna; Niittymaeki, Jaana; Raebinae, Jarkko
PATENT ASSIGNEE(S): Medicel Oy, Finland
SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1199364	A2	20020424	EP 2001-660180	20010925
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
FI 2000002114	A	20020327	FI 2000-2114	20000926
US 2002058313	A1	20020516	US 2001-962805	20010926

PRIORITY APPLN. INFO.: FI 2000-2114 A 20000926

AB Use of recombinant enzymes for the prepn. of GDP-L-fucose and fucosylated glycans is disclosed. GDP-L-fucose functions as a fucose donor in the biosynthetic route leading to the fucosylated glycans, which have therapeutic utility. A process for prepg. GDP-L-fucose and fucosylated glycans, and means useful in the process are provided. Said means include enzymes, chimeric enzymes, DNA sequences, genes, vectors and host cells. Fucosylation of glycans on glycoproteins and -lipids requires the enzymic activity of relevant **fucosyltransferases** and GDP-L-fucose as the donor. Due to the biol. importance of fucosylated glycans, a readily accessible source of GDP-L-fucose would be required. Here the authors describe the construction of a stable recombinant S.cerevisiae strain expressing the E.coli genes gmd and wcaG encoding the two enzymes, GDP-mannose-4,6-dehydratase (GMD) and GDP-4-keto-6-deoxy-D-mannose-3,5-epimerase/4-reductase (GFS) resp., needed to convert GDP-mannose to GDP-fucose via the de novo pathway. Taking advantage of the rich inherent cytosolic GDP-mannose pool in S.cerevisiae cells the authors produced 0.2 mg/l of GDP-L-fucose with the recombinant yeast strain without addn. of any external GDP-mannose. The GDP-L-fucose product may be used as the fucose donor for .alpha.-1,3-**fucosyltransferase** to synthesize sialyl **Lewis x** (sLex), a glycan crucial for the selectin-dependent leukocyte traffic. GDP-L-fucose may also be prepd. using the salvage pathway from L-fucose by fucokinase (FK) and GDP-fucose-pyrophosphorylase (PP), synthesized from a chimeric gene. Two rapid and simple procedures for the quant. anal. of GDP-L-fucose (GDP-Fuc) are described. The methods are based on time-resolved fluorescence and microplate assay technol. The first assay relies on measuring the enzyme activity of .alpha.-1,3-**fucosyltransferase**. In this assay, transfer of fucose from GDP-Fuc converts sialyllactosamine to sialyl **Lewis x** tetrasaccharide, which is detected and quantified by relevant antibodies on a microplate. The formation of the reaction product is directly dependent on the presence of GDP-Fuc in the concn. range of 10-10,000 nM. In the second method GDP-Fuc inhibits the binding of fucose-specific Aleuria aurantia lectin to fucosylated glycan on a microwell. The lectin-based assay is less sensitive than the enzyme

assay, but it is cheaper and faster. The authors used these assays in monitoring the amt. of GDP-Fuc in crude lysates of transgenic yeast, which expresses the enzymes producing GDP-Fuc. The newly developed assays are versatile and applicable to measure also other nucleotide sugars or glycosyltransferase activities in a high-throughput manner.

L5 ANSWER 2 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 1
ACCESSION NUMBER: 2002191218 EMBASE
TITLE: **Helicobacter** priori does not require **Lewis X** or Lewis Y expression to colonize C3H/HeJ mice.
AUTHOR: Takata T.; El-Omar E.; Camorlinga M.; Thompson S.A.; Minohara Y.; Ernst P.B.; Blaser M.J.
CORPORATE SOURCE: T. Takata, First Dept. of Internal Medicine, School of Medicine, Fukuoka University, 7-45-1 Nanakuma, Jonan-Ku, Fukuoka 814-0180, Japan. takatt01@med.nyu.edu
SOURCE: Infection and Immunity, (2002) 70/6 (3073-3079).
Refs: 39
ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Helicobacter** pylori strains frequently express **Lewis X** (Le(x)) and/or Le(y) on their cell surfaces as constituents of the O antigens of their lipopolysaccharide molecules. To assess the effect of Le(x) and Ley expression on the ability of H. pylori to colonize the mouse stomach and to adhere to epithelial cells, isogenic mutants were created in which fucT1 alone or fucT1 and fucT2, which encode the fucosyl transferases necessary for Le(x) and Le(y) expression, were deleted. C3H/HeJ mice were experimentally challenged with either wild-type 26695 H. pylori or its isogenic mutants. All strains, whether passaged in the laboratory or recovered after mouse passage, colonized the mice well and without consistent differences. During colonization by the mutants, there was no reversion to wild type. Similarly, adherence to AGS and KatoIII cells was unaffected by the mutations. Together, these findings indicate that Le expression is not necessary for mouse gastric colonization or for H. pylori adherence to epithelial cells.

L5 ANSWER 3 OF 15 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2001:478310 SCISEARCH
THE GENUINE ARTICLE: 441AY
TITLE: Heterologous over-expression of alpha-1,6-**fucosyltransferase** from Rhizobium sp.: Application to the synthesis of the trisaccharide beta-D-GlcNAc(1 -> 4)-[alpha-L-Fuc-(1 -> 6)]-D-GlcNAc, study of the acceptor specificity and evaluation of polyhydroxylated indolizidines as inhibitors
AUTHOR: Bastida A; Fernandez-Mayoralas A; Arrayas R G; Iradier F; Carretero J C; Garcia-Junceda E (Reprint)
CORPORATE SOURCE: CSIC, Inst Quim Organ Gen, Dept Quim Organ Biol, Juan Cierva 3, E-28006 Madrid, Spain (Reprint); CSIC, Inst Quim Organ Gen, Dept Quim Organ Biol, E-28006 Madrid, Spain; Univ Autonoma Madrid, Fac Ciencias, Dept Quim Organ, E-28049 Madrid, Spain
COUNTRY OF AUTHOR: Spain
SOURCE: CHEMISTRY-A EUROPEAN JOURNAL, (1 JUN 2001) Vol. 7, No. 11, pp. 2390-2397.
Publisher: WILEY-V C H VERLAG GMBH, PO BOX 10 11 61, D-69451 BERLIN, GERMANY.
ISSN: 0947-6539.

DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 78
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB An efficient heterologous expression system fur overproduction of the enzyme alpha -1,6-**Fucosyltransferase** (alpha -1,6-FucT) from Rhizobium sp, has been developed. The gene codifying for the alpha -1.6-FucT was amplified by PCR using specific primers. After **purification**, the gene was cloned in the plasmid pKK2233. The resulting plasmid, pKK1.6FucT, was transformed into the E. coli strain XL1-Blue MRF'. The protein was expressed both as inclusion bodies and in soluble form. Changing the induction time a five-fold increase of enzyme expressed in soluble form was obtained. In this way five units of enzyme alpha -1,6-FucT can be obtained per liter of culture. A crude preparation of the recombinant enzyme was used for the synthesis of the branched trisaccharide alpha -D-GlcNAc-(1 --> 4)-[alpha -L-Fuc-(1 --> 6)]-D-GlcNAc (3), from chitobiose (2) and GDP-Fucose (1). After **purification**, the trisaccharide 3 was obtained in a 84% overall yield. In order to elucidate the structural requirements for the acceptors, the specificity of the enzyme was studied towards mono-, di- and trisaccharides, which are structurally related to chitobiose. The enzyme uses, among others, the disaccharide N-acetyl lactosamine as a good substrate: the monosaccharide GlcNAc is a weak acceptor. Finally, several racemic polyhydroxylated indolizidines have been tested as potential inhibitors of the enzyme. Indolizidine 21 was the best inhibitor with an IC50 of 4.5 x 10(-5) M. Interestingly, this compound turned out to be the best mimic For the structural features of the fucose moiety in the presumed transition state.

L5 ANSWER 4 OF 15 MEDLINE
ACCESSION NUMBER: 2002341969 MEDLINE
DOCUMENT NUMBER: 22079564 PubMed ID: 12084982
TITLE: In vivo fucosylation of lacto-N-neotetraose and lacto-N-neohexaose by heterologous expression of **Helicobacter** pylori alpha-1,3 **fucosyltransferase** in engineered Escherichia coli.
AUTHOR: Dumon C; Priem B; Martin S L; Heyraud A; Bosso C; Samain E
CORPORATE SOURCE: Centre de Recherches sur les Macromolecules Vegetales, 601 rue de la Chimie, BP53X, 38041 Grenoble cedex 09, France.
SOURCE: GLYCOCONJUGATE JOURNAL, (2001 Jun) 18 (6) 465-74. Journal code: 8603310. ISSN: 0282-0080.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020627
Last Updated on STN: 20021004
Entered Medline: 20021003

AB We report here the in vivo production of type 2 fucosylated-N-acetyllactosamine oligosaccharides in Escherichia coli. Lacto-N-neofucopentaose Galbeta1-4GlcNAcbeta1-3Galbeta1-4(Fucalpha1-3)Glc, lacto-N-neodifucohexaose Galbeta1-4(Fucalpha1-3)Glc-NAcbeta1-3Galbeta1-4(Fucalpha1-3)Glc, and lacto-N-neodifucooctaose Galbeta1-4GlcNAcbeta1-3Galbeta1-4(Fucalpha1-3)GlcNAcbeta1-3Galbeta1-4(Fucalpha1-3)Glc were produced from lactose added in the culture medium. Two of them carry the **Lewis X** human antigen. High cell density cultivation allowed obtaining several grams of fucosylated oligosaccharides per liter of culture. The fucosylation reaction was catalyzed by an alpha-1,3 **fucosyltransferase** of **Helicobacter** pylori overexpressed in E. coli with the genes lgtAB of N. meningitidis. The strain was genetically engineered in order to provide GDP-fucose to the system, by genomic inactivation of gene wcaJ involved in colanic acid synthesis and overexpression of RcsA, positive regulator of the colanic acid operon.To prevent fucosylation at the glucosyl residue, lactulose Galbeta1-4Fru was

assayed in replacement of lactose. Lactulose-derived oligosaccharides carrying fucose were synthesized and characterized. Fucosylation of the fructosyl residue was observed, indicating a poor acceptor specificity of the **fucosyltransferase** of H. pylori.

L5 ANSWER 5 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:201412 BIOSIS
DOCUMENT NUMBER: PREV200200201412
TITLE: The role of redundant alpha-3-**fucosyltransferase** genes futA and futB in Lewis antigen x/y synthesis by **Helicobacter** pylori.
AUTHOR(S): Baker, P. E. (1); Rosenberg, J. B. (1); Mefford, M. E.; Thevenot, T. L.
CORPORATE SOURCE: (1) Ohio State University, Columbus, OH USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 292. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print. Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001 ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The gastric pathogen H. pylori expresses two alpha-3-**fucosyltransferases**, which may play different roles in the synthesis of Lewis antigens on H. pylori lipopolysaccharide (LPS). These enzymes are encoded by futA and futB, which contain poly(C) regions vulnerable to slip-strand mispairing during replication. The purpose of this study was to determine the relationship of futA and futB expression with Lewis antigen phenotype and animal colonization. futA and futB were amplified from lab-passed and animal-passed H. pylori strains. The resultant PCR products were sequenced and the length of the poly(C) tract was determined. In addition, antibodies specific for **Lewis x** or Lewis y antigens were used to determine the LPS phenotype by western blot and ELISA. In the two animal-virulent strains examined, SS1 and 26695, there was no relationship between futA sequence, **Lewis x** or y expression, or animal passage. The length of the poly(C) region of futA varied between strains and between **isolates** of the same strain, but a relationship between the on/off status of the gene and bacterial phenotype could not be established. In contrast, futB expression was more stable. Variations were present in the poly(C) tract, but predicted amino acid sequence revealed that the gene was still expressed. Like futA, futB expression did not correlate with **Lewis x** expression, but because both futB and Lewis y were expressed in all strains, no relationship could be determined. When **isolates** of the same strain were compared, there was no relationship between futB expression and animal virulence. However, pig and mouse virulent strains differed from each other. Pig strains expressed both Lewis antigens (regardless of level of virulence), while mouse strains expressed only Lewis y. In animal virulent strains of H. pylori futB appears to be sufficient for **Lewis x**/y synthesis, but futA is not necessary. Furthermore, neither futA nor **Lewis x** determine level of virulence of an individual strain for its host. The role of **Lewis x** and y in determining host species specificity will require further investigation.

L5 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:314847 CAPLUS
DOCUMENT NUMBER: 132:330636
TITLE: Sequences of **Helicobacter** pylori .alpha.1,2-**fucosyltransferase**, and uses thereof in diagnosing disorders and in monitoring diseases
INVENTOR(S): Taylor, Diane E.; Wang, Ge; Palcic, Monica
PATENT ASSIGNEE(S): Governors of the University of Alberta, Can.
SOURCE: PCT Int. Appl., 71 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000026383	A1	20000511	WO 1999-CA1031	19991103
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6238894	B1	20010529	US 1999-433598	19991102
EP 1127138	A1	20010829	EP 1999-953470	19991103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002528122	T2	20020903	JP 2000-579755	19991103
US 2002037570	A1	20020328	US 2001-848838	20010503

PRIORITY APPLN. INFO.:
US 1998-107268P P 19981104
US 1999-433598 A 19991102
WO 1999-CA1031 W 19991103

OTHER SOURCE(S): MARPAT 132:330636

AB This invention provides protein and DNA sequences for a newly identified **Helicobacter** pylori .alpha.1,2-**fucosyltransferase**, which is involved in biosynthesis of fucosylated oligosaccharides including **Lewis X**, Lewis Y, Lewis B and H type 1, which are structurally similar to certain tumor-assocd. carbohydrate antigens found in mammals. The center region of fucT2 gene has a sequence of TAA repeats immediately following the poly C sequence, which are hypermutable and could offer an on-off mechanism for the expression of the gene, and changes of the repeat no. of the both tracts contribute to the variation of the fucT2 genotype in different strains. The invention further provides a method to measure the enzymic activity and acceptor specificity of .alpha.1,2-**fucosyltransferase**. The invention also relates to .alpha.1,2-**fucosyltransferase** antibodies which have research and diagnostic utility in the development of assays to detect mammalian tumors.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 2000:148527 CAPLUS
DOCUMENT NUMBER: 132:290436
TITLE: Cloning and characterization of the .alpha.(1,3/4) **fucosyltransferase** of **Helicobacter** pylori
AUTHOR(S): Rasko, David A.; Wang, Ge; Palcic, Monica M.; Taylor, Diane E.
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, University of Alberta, Edmonton, AB, T6G 2H7, Can.
SOURCE: Journal of Biological Chemistry (2000), 275(7), 4988-4994
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The gastric pathogen **Helicobacter** pylori can express the histo

blood group antigens, which are on the surface of many human cells. Most H. pylori strains express the type II carbohydrates, **Lewis X** and Y, whereas a small population express the type I carbohydrates, Lewis A and B. The expression of Lewis A and **Lewis X**, as in the case of H. pylori strain UA948, requires the addn. of fucose in .alpha.1,4 and .alpha.1,3 linkages to type I or type II carbohydrate backbones, resp. This work describes the cloning and characterization of a single H. pylori **fucosyltransferase** (FucT) enzyme, which has the ability to transfer fucose to both of the aforementioned linkages in a manner similar to the human **fucosyltransferase** V (Fuc-TV). Two homologous copies of the fucT gene have been identified in each of the genomes sequenced. The characteristic adenosine and cytosine tracts in the amino terminus and repeated regions in the carboxyl terminus are present in the DNA encoding the two UA948fucT genes, but these genes also contain differences when compared with previously identified H. pylori fucTs. The UA948fucTa gene encodes an approx. 52-kDa protein contg. 475 amino acids, whereas UA948fucTb does not encode a full-length FucT protein. In vitro, UA948FucTa appears to add fucose with a greater than 5-fold preference for type II chains but still retains significant activity using type I acceptors. The addn. of the fucose to the type II carbohydrate acceptors, by UA948FucTa, does not appear to be affected by fucosylation at other sites on the carbohydrate acceptor, but the rate of fucose transfer is affected by terminal fucosylation of type I acceptors. Through mutational anal. we demonstrate that only FucTa is active in this H. pylori **isolate** and that inactivation of this enzyme eliminates expression of all Lewis antigens.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3

ACCESSION NUMBER: 1999:651501 CAPLUS
DOCUMENT NUMBER: 132:1916
TITLE: Phase variation in **Helicobacter** pylori lipopolysaccharide due to changes in the lengths of Poly(C) tracts in .alpha.3-**fucosyltransferase** genes
AUTHOR(S): Appelmelk, Ben J.; Martin, Steve L.; Monteiro, Mario A.; Clayton, Chris A.; McColm, Andrew A.; Zheng, Pengyuan; Verboom, Theo; Maaskant, Janneke J.; Van den Eijnden, Dirk H.; Hokke, Cornelis H.; Perry, Malcolm B.; Vandenbroucke-Grauls, Christina M. J. E.; Kusters, Johannes G.
CORPORATE SOURCE: Departments of Medical Microbiology, Vrije Universiteit, Medical School, Amsterdam, 1081 BT, Neth.
SOURCE: Infection and Immunity (1999), 67(10), 5361-5366
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The lipopolysaccharide (LPS) of **Helicobacter** pylori expresses the **Lewis x** (Lex) and/or Ley antigen. It was shown previously that H. pylori LPS displays phase variation whereby an Lex-pos. strain yields variants with different LPS serotypes, for example, Lex plus Ley or nonfucosylated polylactosamine. H. pylori has two .alpha.3-**fucosyltransferase** genes that both contain poly(C) tracts. We now demonstrate that these tracts can shorten or lengthen randomly, which results in reversible frameshifting and inactivation of the gene products. We provide genetic and serol. evidence that this mechanism causes H. pylori LPS phase variation and demonstrate that the on or off status of .alpha.3-**fucosyltransferase** genes dets. the LPS serotypes of phase variants and clin. **isolates**. The role of the .alpha.3-**fucosyltransferase** gene products in detg. the LPS serotype was

confirmed by structural-chem. anal. of .alpha.3-**fucosyltransferase** knockout mutants. The data also show that the two .alpha.3-**fucosyltransferase** genes code for enzymes with different fine specificities, and we propose the names futA and futB to designate the orthologs of the H. pylori 26695 .alpha.3-**fucosyltransferase** genes HP0379 and HP0651, resp. The data also show that the .alpha.3-fucosylation in H. pylori precedes .alpha.3-**fucosyltransferase**, an order of events opposite to that which prevails in mammals. Finally, the data provide an understanding at the mol. level of the mechanisms underlying LPS diversity in H. pylori, which may play an important role in adaptation to the host.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 15 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1999:890888 SCISEARCH
THE GENUINE ARTICLE: 255GA
TITLE: Novel **Helicobacter** pylori alpha 1,2-**fucosyltransferase**, a key enzyme in the synthesis of Lewis antigens
AUTHOR: Wang G; Boulton P G; Chan N W C; Palcic M M; Taylor D E (Reprint)
CORPORATE SOURCE: UNIV ALBERTA, DEPT MED MICROBIOL, EDMONTON, AB T6G 2H7, CANADA (Reprint); UNIV ALBERTA, DEPT MED MICROBIOL, EDMONTON, AB T6G 2H7, CANADA; UNIV ALBERTA, DEPT IMMUNOL, EDMONTON, AB T6G 2H7, CANADA; UNIV ALBERTA, DEPT CHEM, EDMONTON, AB T6G 2H7, CANADA
COUNTRY OF AUTHOR: CANADA
SOURCE: MICROBIOLOGY-UK, (NOV 1999) Vol. 145, Part 11, pp. 3245-3253.
Publisher: SOC GENERAL MICROBIOLOGY, MARLBOROUGH HOUSE, BASINGSTOKE RD, SPENCERS WOODS, READING RG7 1AE, BERKS, ENGLAND.
ISSN: 1350-0872.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 33

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Helicobacter** pylori lipopolysaccharides (LPS) contain complex carbohydrates known as Lewis antigens which may contribute to the pathogenesis and adaptation of the bacterium. Involved in the biosynthesis of Lewis antigens is an alpha 1,2-**fucosyltransferase** (FucT) that adds fucose to the terminal beta Gal unit of the O-chain of LPS, Recently, the H, pylori (Hp) alpha 1,2-fucT-encoding gene (fucT2) was cloned and analysed in detail. However, due to the low level of expression and instability of the protein, its enzymic activity was not demonstrated. In this study, the Hp fucT2 gene was successfully overexpressed in Escherichia coli, Sufficient amounts of the protein were obtained which revealed alpha 1,2-**fucosyltransferase** activity to be associated with the protein. A series of substrates were chosen to examine the acceptor specificity of Hp alpha 1,2-fucT, and the enzyme reaction products were identified by capillary electrophoresis. In contrast to the normal mammalian alpha 1,2-FucT (H or Se enzyme), Hp alpha 1,2-FucT prefers to use **Lewis X** [beta Gal1-4(alpha Fuc1-3)beta GlcNAc] rather than LacNAc [beta Gal1-4 beta GlcNAc] as a substrate, suggesting that H, pylori uses a novel pathway (via **Lewis X**) to synthesize Lewis Y. Hp alpha 1,2-FucT also acts on type 1 acceptor [beta Gal1-3 beta GlcNAc] and Lewis a [beta Gal1-3(alpha Fuc1-4)beta GlcNAc], which provides H, pylori with the potential to synthesize H type 1 and Lewis b epitopes. The ability to transfer fucose to a monofucosylated substrate (**Lewis X** or Lewis a) makes Hp alpha 1,2-FucT distinct from normal mammalian alpha 1,2-FucT.